Application No. 10/019,816
Filed: March 27, 2002
TC Art Unit: 1642
Confirmation No.: 9944

REMARKS

The pending claims in the above-identified application have been subjected to a restriction requirement, the Examiner saying that the claims lack unity of invention. The Applicants traverse the restriction requirement for the reasons given below, and reconsideration is requested. If the Examiner maintains the restriction requirement, the Applicants elect the claims of Group 4, claims 217-225, 236-238 and 240-246, with traverse, for prosecution at this time.

The claims remaining in the application have been amended, without prejudice, to define the administered agent as binding to the MAP kinase or cytoplasmic region of an integrin in order to progress the application. Support for these amendments is found in the specification at, for instance, page 12, lines 11 to 16 and page 46, line 8 to page 47, line 2. New claims (247-262) are subsets of the Group 4 claims, and support is found for these claims throughout the specification as originally filed. Applicants' cancellation of certain rejected claims is not to be construed as an admission that the Examiner's rejections were proper. The Applicants continue to believe that the rejected claims are described in and enabled by the specification, and are

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
TEL. (617) 542-2290

not obvious in view of the cited references. The rejected claims have been cancelled for the sole purpose of advancing the case to allowance. If the restriction requirement is maintained, the Applicants plan to file divisional application(s) to continue the prosecution of the rejected claims.

With regard to the Pillinger and the Gu articles cited by the Examiner, both citations refer to integrin-mediated signalling via the conventional Ras/Raf/MEK/ERK mitogen-activated protein kinase (MAPK) activation pathway. The conventional MAPK activation pathway is illustrated in the attached diagram. The integrin is the transmembrane protein with subunits numbered 1 and 2. As shown in the diagram, the MAP kinase is activated remotely from the integrin. In contrast, the present invention relates to the finding that MAP kinases such as ERK can bind directly to the cytoplasmic region of integrins and that by inhibiting this interaction, cellular activity can be modulated. Neither Pillinger nor Gu teachs or suggests that a MAP kinase may bind directly to a cytoplasmic region of an integrin; nor does either of these prior art documents teach or suggest administering an agent that binds to the MAP kinase or integrin and thereby inhibits the MAP kinase-integrin binding interaction as now claimed.

More particularly, Pillinger relates to a study indicating a role for ERK in CD11b/CD18 integrin-dependent neutrophil adhesion and that salicylates may inhibit ERK signalling. As stated at page 14544, Col. 2, lines 19 to 27, the cited reference teaches that the observed salicylate ERK inhibition was likely due to disruption of ERK activating pathways *within the cell membrane* as a result of the ability of salicylates to intercalate into the plasma membrane and disrupt receptor/target interactions or alternatively, G protein to *Ras* and/or *Raf-1* activation. Indeed, Pillinger states that it is unlikely that cytoplasmic domains of CD11b/CD18 molecules serve as direct substrates for ERK (see page 14543, Col. 2, lines 9 to 19) and so teaches away from the present invention.

Gu relates to a study indicating that expression of the tumor suppressor PTEN protein selectively inhibits activation of the MAPK activation pathway and suggests that the sites of action of PTEN are on (a) *Shc* and its interaction with the adaptor protein *Grb2* and (b) focal adhesion kinase (FAK), as stated at page 1382, Col. 1, final paragraph of Gu. Again, this citation neither teaches nor suggests direct binding of a MAP kinase with an integrin, nor inhibition of this binding interaction to modulate cellular activity.

Application No. 10/019,816
Filed: March 27, 2002
TC Art Unit: 1642
Confirmation No.: 9944

Thus, the Applicants submit that the Examiner's anticipation argument has been overcome and that the claims of Groups 1-4 do relate to a single general inventive concept. The Applicants submit, further, that all claims in the application are in condition for allowance and such action is requested.

The Examiner is encouraged to telephone the undersigned attorney to discuss any matter that would expedite allowance of the present application.

Respectfully submitted,

MICHAEL V. AGREZ, ET AL.

By: Holliday C. Heine

Holliday C. Heine, Ph.D.
Registration No. 34,346
Attorney for Applicant(s)

WEINGARTEN, SCHURGIN,
GAGNEBIN & LEBOVICI LLP
Ten Post Office Square
Boston, MA 02109
Telephone: (617) 542-2290
Telecopier: (617) 451-0313

HCH/jms
315235